

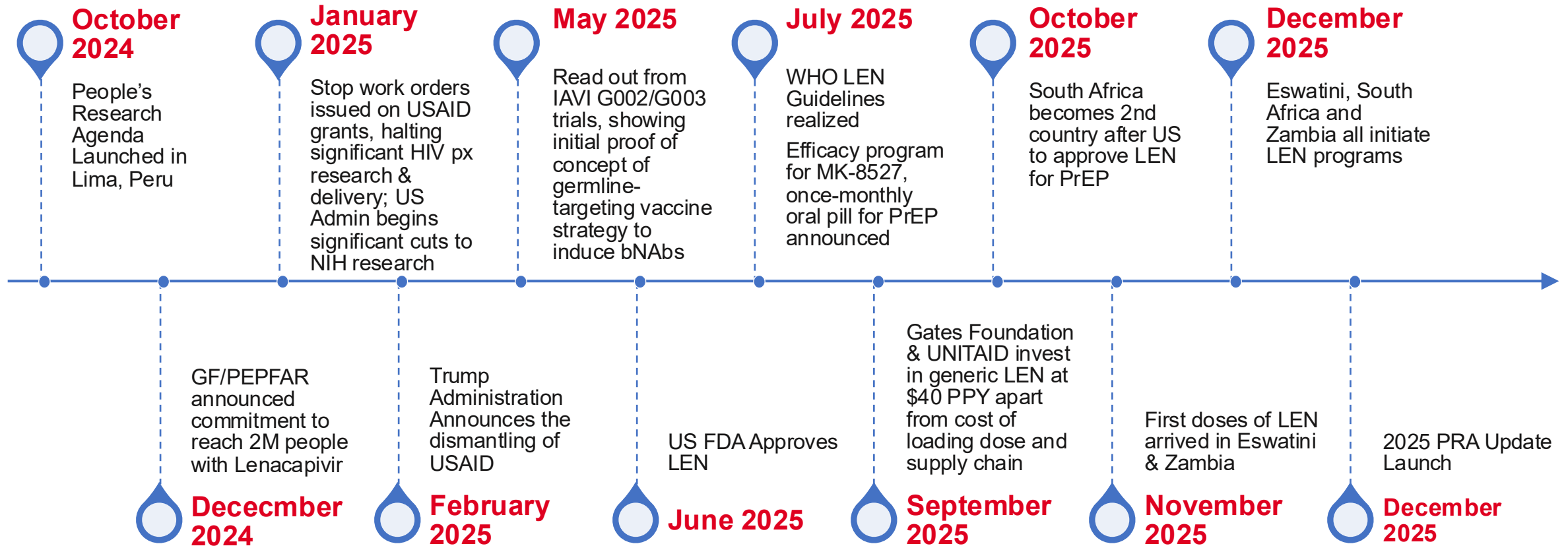


PEOPLE'S RESEARCH AGENDA

2025 Update: HIV Prevention R&D at a Crossroads

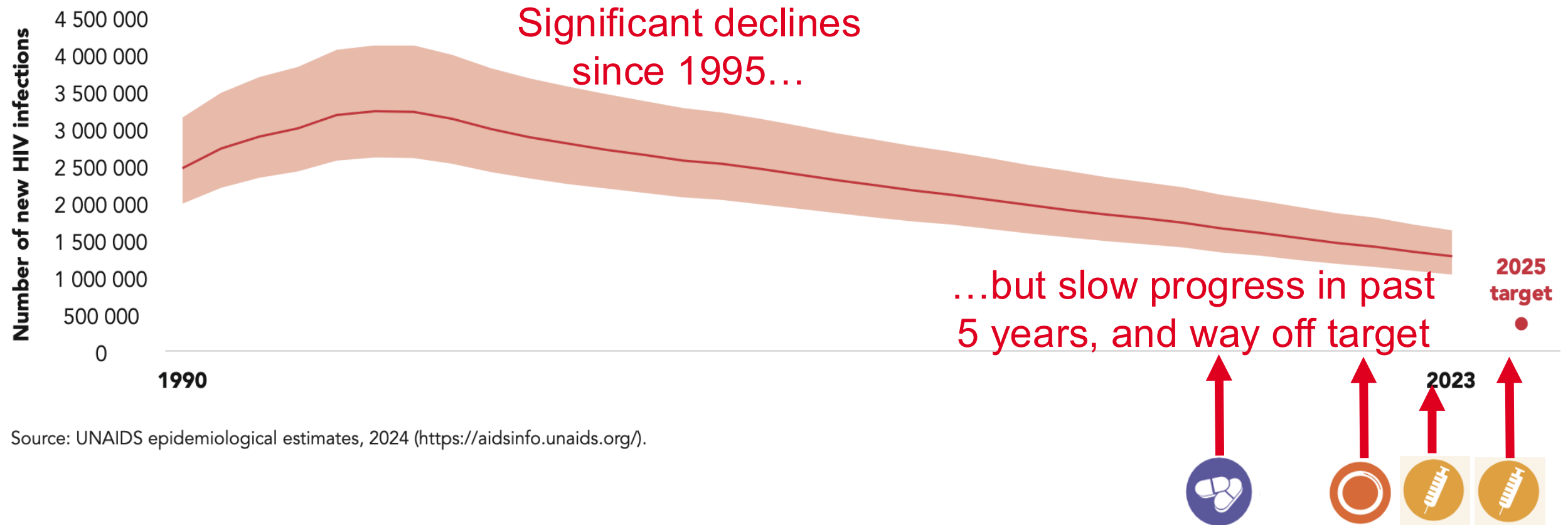
20 January 2026

Since the 2024 PRA Launch in Lima....





























The Big Picture?

Figure 0.1 Number of new HIV infections, global, 1990–2023, and 2025 target




Source: UNAIDS epidemiological estimates, 2024 (<https://aidsinfo.unaids.org/>).

People's Research Agenda 2025 Update

PRECLINICAL	PHASE I	PHASE II	PHASE III	IMPLEMENTATION
<p>Hundreds of...</p> <ul style="list-style-type: none">  ARV-Based  MPTs  Vax candidates  bNAbs candidates <p>The termination of the MATRIX project has resulted in a pipeline that lacks on-demand products and delivery platforms, plus multi-purpose prevention technologies (MPTs). Multiple early-stage vaccine candidates were also discontinued with the termination of BRILLIANT and ADVANCE.</p> <ul style="list-style-type: none">  Long-acting implants  Multi-purpose vaginal ring  Vaginal & mucosal inserts  Vaginal film  Vaccines 	<ul style="list-style-type: none">  3-Monthly DPV  On-Demand TAF + EVG  21 vax candidates  3 combo bNAb candidates 	<ul style="list-style-type: none">  Event-Driven F/TAF  3-Monthly DPV + LNG  Daily DPP  4-Monthly CAB  On-Demand TFV  2 combo bNAb candidates 	<ul style="list-style-type: none">  Monthly MK-8527  12-Monthly LEN 	<ul style="list-style-type: none">  Daily TDF/FTC  Daily F/TAF  2-Monthly CAB  6-Monthly LEN  Monthly DPV

KEY:

-  ARV-based
-  MPTs
-  Vaccines
-  bNAbs

bNAb: broadly-neutralizing antibodies, CAB: Cabotegravir, DPP: dual prevention pill, DPV: Dapivirine, EVG: Elvitegravir, F/TAF: emtricitabine/tenofovir alafenamide, LEN: Lenacapavir, LNG: Levonorgestrel, TAF: tenofovir alafenamide, TDF/FTC: tenofovir disoproxil fumarate-emtricitabine

- Funding cuts brought People's Research Agenda in Crisis – outlined priorities are all under threat; potential for irrevocable damage to critical aspects of research, choice, access
- First annual update launched an interactive report, live pipeline tracker, highlight gaps and priorities for the field in the current time
- Maps the advocacy path forward for 2026

People's Research Agenda Update: Summary Table

Modality	Status (2025)	Gaps	2026 Priorities
ARV-based Prevention	<ul style="list-style-type: none"> • <u>Ongoing rollout of daily oral, CAB, and DVR</u> • <u>Ongoing momentum with LEN approvals, accelerated roll out and market shaping</u> - potential intro in <u>12 priority countries</u> by Q1 2026 • <u>Launch of oral monthly pill (MK-8527) Phase III trials in 17 countries</u> • Research progress towards 12-month dosing cycles for LEN, 4-monthly CAB, and 90-day ring 	<ul style="list-style-type: none"> • Slow scale-up of proven options (oral PrEP, injectable CAB, DVR) • <u>Funding cuts disrupting pipeline diversification</u> • Missing on-demand and short-acting prevention products in prevention toolbox 	<ul style="list-style-type: none"> • Accelerate implementation and optimization of existing PrEP options • Innovate community-led delivery platforms and differentiated service delivery models • Define market segmentation for multiple LA regimens • Maintain community engagement and regulatory readiness for rapid rollout of new products • Re-balance product pipeline • <u>GPP/ongoing engagement for MK-8527 program</u>
Multi-Purpose Prevention Technologies (MPTs)	<ul style="list-style-type: none"> • Pipeline mostly in pre-clinical/early phase • <u>DPP the most advanced MPT</u>; Phase IIb acceptability study ongoing • <u>Other MPT products stalled by USAID cuts, including MATRIX product pipeline</u> 	<ul style="list-style-type: none"> • Funding uncertainty for key products, including vaginal film and fasting dissolving inserts • Limited products for gender-diverse populations • Complexities around manufacturing and regulatory pathways • Limited STI prevention integration 	<ul style="list-style-type: none"> • Develop investment case for paused MPT products to funders • Expand pipeline beyond ARV-based products and cis-women population • Engage regulators, WHO, and advocates early to define combination-product pathways • <u>Build on lessons learnt from DPP market shaping, conversation for future MPT products</u>
Vaccines	<ul style="list-style-type: none"> • Most studies in early phase focusing on germline-targeting, inducing T-cells, and mRNA approaches • 6 small trials started under HVTN despite funding cut threats • <u>Uncertainty about NIH support for HIV vaccine R&D-e.g. CHAVD threats</u> • <u>USAID terminated ADVANCE and BRILLIANT programs</u> • Growing vaccine hesitancy, mis- and disinformation 	<ul style="list-style-type: none"> • Lacking consensus on TPP • Lack of clarity on interim milestones for success • Risks to R&D infrastructure in high burden regions • Weakening political/public support 	<ul style="list-style-type: none"> • Align and socialize updated HIV vaccine TPP • Create coordinated R&D roadmap with clear milestones • Rebuild advocacy to sustain funding and counter misinformation • Invest in regulatory, trial, and manufacturing capacity in high-burden regions - Africa, Asia, Latin America
Broadly Neutralizing Antibodies (bNAbs)	<ul style="list-style-type: none"> • Ongoing progress toward combo bNAbs ("combo AMP") • Early trials testing potency, breadth, and duration of different combos • Ongoing focus on infant prophylaxis and combo formulations • Attempts to define market pathways 	<ul style="list-style-type: none"> • Unclear role and market use case as an actual product • Complex manufacturing/delivery • No defined commercialization or access path 	<ul style="list-style-type: none"> • Reach consensus on bNAb use cases and update TPPs • Clarify development and regulatory pathways • Define commercial-partner strategy • Sustain civil society dialogue on potential role of bNAbs
Cross-cutting	<ul style="list-style-type: none"> • Funding contractions reshaping priorities without community input • Shifting focus to implementation science at expense of discovery science and product development • Complexity of conducting traditional randomized controlled trials in current prevention landscape • Widespread uncertainty and instability threaten future efforts 	<ul style="list-style-type: none"> • Invest across basic research, clinical trials, and implementation science, avoiding duplication and prioritizing unmet needs • Embed meaningful community engagement & GPP at all stages of research, including trials & implementation • Use adaptive and inclusive trial designs informed by community perspectives, with clear access plans for successful products • Sustain early-phase trial infrastructure to enable future progress 	

From Data to Action: A snapshot for the Interactive PRA

<https://avac.org/peoples-research-agenda/>



HIV PREVENTION PIPELINE: PRODUCTS TO WATCH

Click on each of the prevention options below for more details on the pipeline



- Clinical Trial Information
- Pipeline Tracker
- Infographics
- Factsheet (status, gaps and priorities for the field)
- Priorities for advocacy

PRA PIPELINE TRACKER

This tracker provides details on key HIV prevention trials to watch. It is updated on a quarterly and ad-hoc basis as developments occur. If you would like to share additional information or corrections, please email Breanne at breanne@avac.org.



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Category	Product Name	Trial Name (if available)	Phase	Status	Trial Description	Developer/ Sponsor	Funder/ Partner
PrEP	MK-8527	MK-8527-015	Phase I	Ongoing	Open-Label, Single-Dose Study to Evaluate the Safety and Immunogenicity of AAd4-HIV Envelope Vaccine	Merck	Merck
Vaccine	Three AAd4-vector based vaccines delivered intranasally	19-1-0069	Phase I, Open label	Completed	Open-label, single arm study to evaluate the safety and		NIAID
nAbs	3BNC117-LS, 10-1074-LS Plus N-803 (bNAb-N-803)	3BNC117-LS and 10-1074-LS Plus N-803 (bNAb-N-803)	Phase I, Open-label	Ongoing	Assess whether the administration of two bNAbs	ACTG, HVTN, HPTN	NIAID, DAIDS
nAbs	3BNC117-LS-J, 10-1074-LS-J	A5416/HVTN 806/HPTN 108 (PAUSE study)	Phase I	Ongoing	Randomized double-blind, placebo-controlled phase 2	ACTG	NIAID, DAIDS
nAbs	10-1074-LS, 3BNC117-LS	A5417or ACACIA	Phase II	Ongoing			
Vaccine	Prime-boost BG505 GT1.1-SMNP adjuvant +	BRILLIANT-011	Phase I	Planned		BRILLIANT Consortium	Gates Foundation (previous USAID)
nAbs	VRC07-523LS, PGT121	CAPRISA 012A	Phase I	Completed	Assess safety and PK of VRC07-523LS and PGT121	CAPRISA	

People's Research Agenda 2025 Update Summary Table

DECEMBER 2025

[Downloadable version available.](#)

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The Way(s) Forward

Balance and focus	Strategically invest across basic research, clinical trials, and implementation science, avoiding duplication and prioritizing unmet needs
Innovate early	Sustain early-phase trials for vaccines, multipurpose prevention technologies (MPTs), and next-generation products to build an effective toolkit for future HIV prevention
Implementation matters	Invest in real-world studies to optimize delivery, access, and uptake of emerging prevention options, such as long-acting PrEP
Community Engagement	Embed meaningful community engagement and Good Participatory Practices at all stages of research and trials
Design for relevance	Use adaptive, ethical, and inclusive trial designs informed by community perspectives, with clear access plans for successful products

Resources

- [People's Research Agenda \(PRA\)](#)
- [Ongoing rollout of daily oral, CAB and DVR](#)
- [Ongoing momentum with LEN approvals, accelerated roll out and market shaping](#)
- [Launch of oral monthly MK-8527 Phase III trials across 17 countries](#)
- [Getting Rollout Right This Time](#) – insights and best practices for successful PrEP rollout
- [Global PrEP Tracker](#) – tracking PrEP initiations by country over time
- [PrEPWatch.org](#) – data, information, and PrEP resources
- [WHO guidelines released in July 2025](#)
- [From The Lab To The Jab series](#)

The Future of HIV Prevention: Peril & Promise



Jeanne Marrazzo, MD

January 20, 2026

A People's Research Agenda for Speed, Scale and Equity

AVAC Webinar

Today's Discussion

- The current landscape: peril & promise
- Challenges in the field of chemoprophylaxis
 - PEP/PrEP in a time of urgent need
- Exciting advances & opportunities
 - Formulations for chemoprophylaxis, vaccines & monoclonal antibodies
- How will we find a way forward?

OVERCOMING DISRUPTION

Transforming the
AIDS response



WORLD AIDS DAY | 2025

The Global HIV Pandemic

- 9.2 million people living with HIV not on treatment (77% coverage)
- 11 million people living with HIV had unsuppressed viral loads
- 1.3 million people newly acquired HIV in 2024 (2025 goal: <370,000)
- External aid predicted to drop 30–40% between 2023 - 2025, causing immediate & severe disruption to health services
- Funding cuts particularly affect prevention services and people living with HIV, young people, women & key populations of gay men & other men who have sex with men, people who inject drugs, sex workers & transgender persons

In a Landscape Characterized By...Many Perils

- Cuts in US government **funding** & support of global efforts (WHO, PEPFAR)
- **Partner** organizations in disarray (NIH, CDC), threatening collaborative work in public health & discovery, surveillance
- Required compliance with “new” priorities (language & populations) that threaten explicit advocacy for **equity**
- Low public **trust** in vaccines & non-pharmaceutical interventions
- **Workforce** challenges (clinical, research, education), especially with loss of funding & disproportionate effect on trainees



The Trump presidency: Cascading global shocks on global health

Lawrence O. Gostin*



O'Neill Institute for National and Global Health Law, Georgetown University Law Center, Washington, DC, United States of America

* gostin@law.georgetown.edu

November 26, 2025

The world has been experiencing cascading global shocks, tightly interwoven with global health—the COVID-19 pandemic, climate change, conflicts, and humanitarian crises propelling mass migrations. On January 20, 2025, global health experienced a shock of another sort, the inauguration of Donald J. Trump.

On day one, President Trump issued an executive order giving notice of the U.S. intention to withdraw its membership in the World Health Organization (WHO) [1]. While the United States is legally bound to give a year's notice and pay all debts, the president immediately stopped all funding and ordered the U.S. Centers for Disease Control and Prevention (CDC) to cease all communications with WHO. Another executive order that day froze all new obligations and disbursements of foreign assistance funds [2]. Days later, Secretary of State Marco Rubio issued a stop-work order, requiring nearly all ongoing foreign assistance activities to come to an immediate halt [3]. And that was only the first week.

Here and in an avalanche of other unilateral executive actions, the Trump administration has asserted a constitutional vision of the virtually unchecked powers of the presidency. The administration's view of unfettered authority is at odds with the core constitutional principles of separation of powers and checks and balances, as well as with longstanding practice. Yet the U.S. Congress has not pushed back, and the Supreme Court has allowed most of the president's executive actions to take effect as litigation challenging them plays out.

Here, I document key executive actions on global health taken by the Trump administration, and the destructive impacts on global health and U.S. national interests. The executive orders on withdrawing the United States from WHO and freezing foreign aid were most consequential to global health, and will be my primary focus. While numerous executive and legislative actions profoundly impact global health (e.g., climate change, immigration, tariffs, and biomedical research), they are largely beyond this article's scope. I conclude with proposals for using this major rupture in international health cooperation as an opportunity to construct a more resilient global health financing and governance ecosystem. Out of peril there is opportunity for new alliances, self-reliance, and resilience *sans* the United States—at least until the next presidential election in 2028.



Kennedy Fires N.I.H. Scientist Who Filed Whistle-Blower Complaint

Dr. Jeanne Marrazzo, who was on administrative leave, alleged that the Trump administration had defied court orders and undermined vaccine research.



CWRU AIDS Clinical Trials Unit

2d · 🌐

NIH DAIDS Director Carl Dieffenbach Reassigned to Fogarty Center Advisor Role

Carl Dieffenbach, longtime director of the National Institutes of Health's Division of AIDS, has been reassigned to a senior advisor post in the Fogarty International Center's Office of the Director, according to an internal email obtained by Inside Health Policy.

<https://insidehealthpolicy.com/.../nih-aids-division...>



The human impact of disruption

“We have seen an increase in threats towards key populations, this is an attempt to erase our existence,” said Walimbwa of Ishtar MSM, Kenya

“Social support networks of adolescent girls and young women have been weakened,” reported one peer education from Uganda surveyed by the Athena Network.

“Thousands of adolescent girls and young women are now isolated and detached from their networks... the girls are scattered, and this has increased their vulnerability.”

“These programmes empowered me and transformed my life,” said Talent Manyoni following the closure of the DREAMS initiative for adolescent girls and young women in Zimbabwe.



In sub-Saharan Africa SSA new HIV infections declined by:
62% among adolescent boys and young men (15–24 years) and by
51% among adolescent girls and young women (15–24 years)

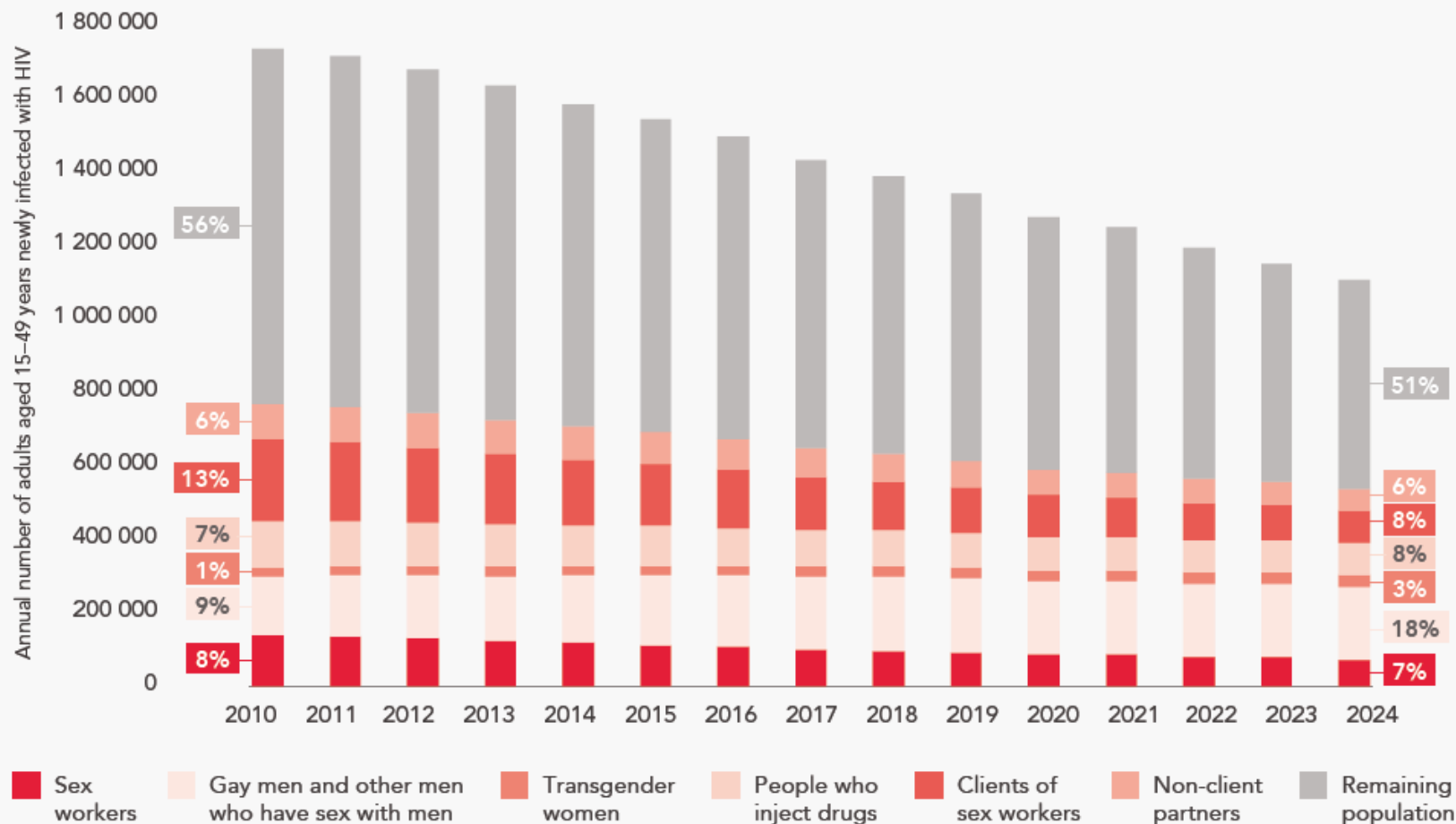


Service disruptions are occurring at a time when the proportion of the HIV burden among some key populations is rising

- Key populations (including clients of sex workers) are less than 6% of the adult 15-49 population, but they and their partners bear 49% of new infections in 2024, up from 44% in 2010.
- Stark inequalities continue to exist in the risk of acquiring HIV compared to the general adult population:
 - 17x greater for sex workers and transgender women
 - 18x greater for men who have sex with men
 - 34x greater for people who inject drugs

FIGURE 1.6

Trends in numbers of new adult HIV infections by population, global, 2010–2024

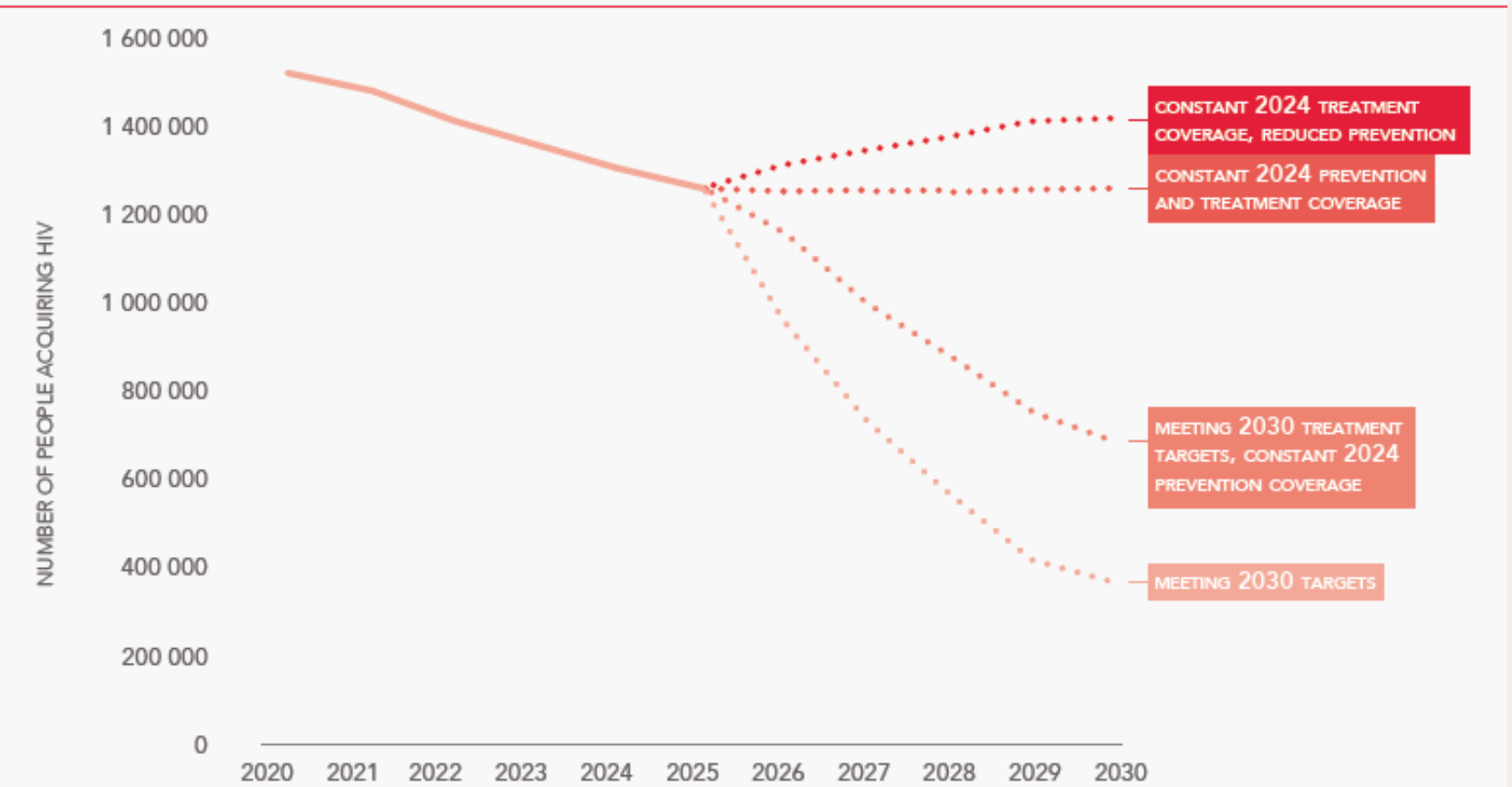


Without renewed commitment, new HIV infections could rise and undermine efforts to end AIDS as a public health threat

- Modelling the impact of these funding cuts, UNAIDS projects that in 2030 there would be 1.4 million annual new HIV infections.
- Over the period 2025-2030 this would result in an additional 3.9 million people newly acquiring HIV, compared to a scenario of reaching the global HIV targets by 2030.

FIGURE 3.1

Figure 3.1. Number of people acquiring HIV, 2020–2024, and projected scenarios, 2025–2030, global.



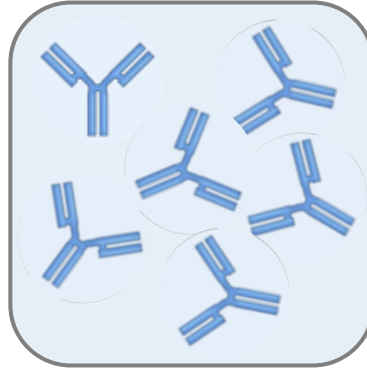
Despite This...New Methods and Modalities for HIV Prevention Offer Great Promise



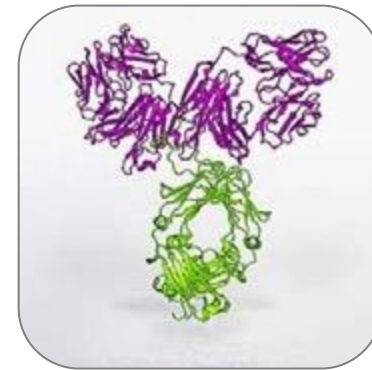
Vaccines



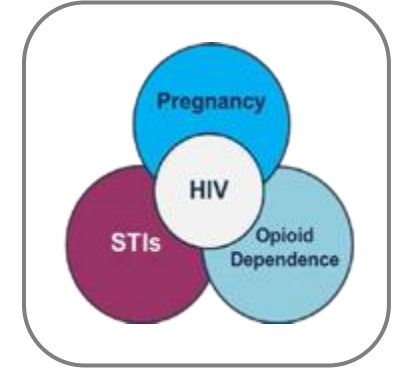
**Novel Long-Acting
ARV Methods and
Delivery Systems**



**Monoclonal
Antibodies**



**Broadly
Neutralizing
Antibodies
(bNAbs)**



















**Multi-purpose
Technologies
(MPTs)**

Overview of Lenacapavir (LEN) for PrEP Trials

- ★ Initial data
- ★ Possible data
- ✓ Possible earliest regulatory submissions
- ✓ Possible earliest regulatory approval and market entry with product from Gilead
- ★ Possible earliest generic manufacturer(s)

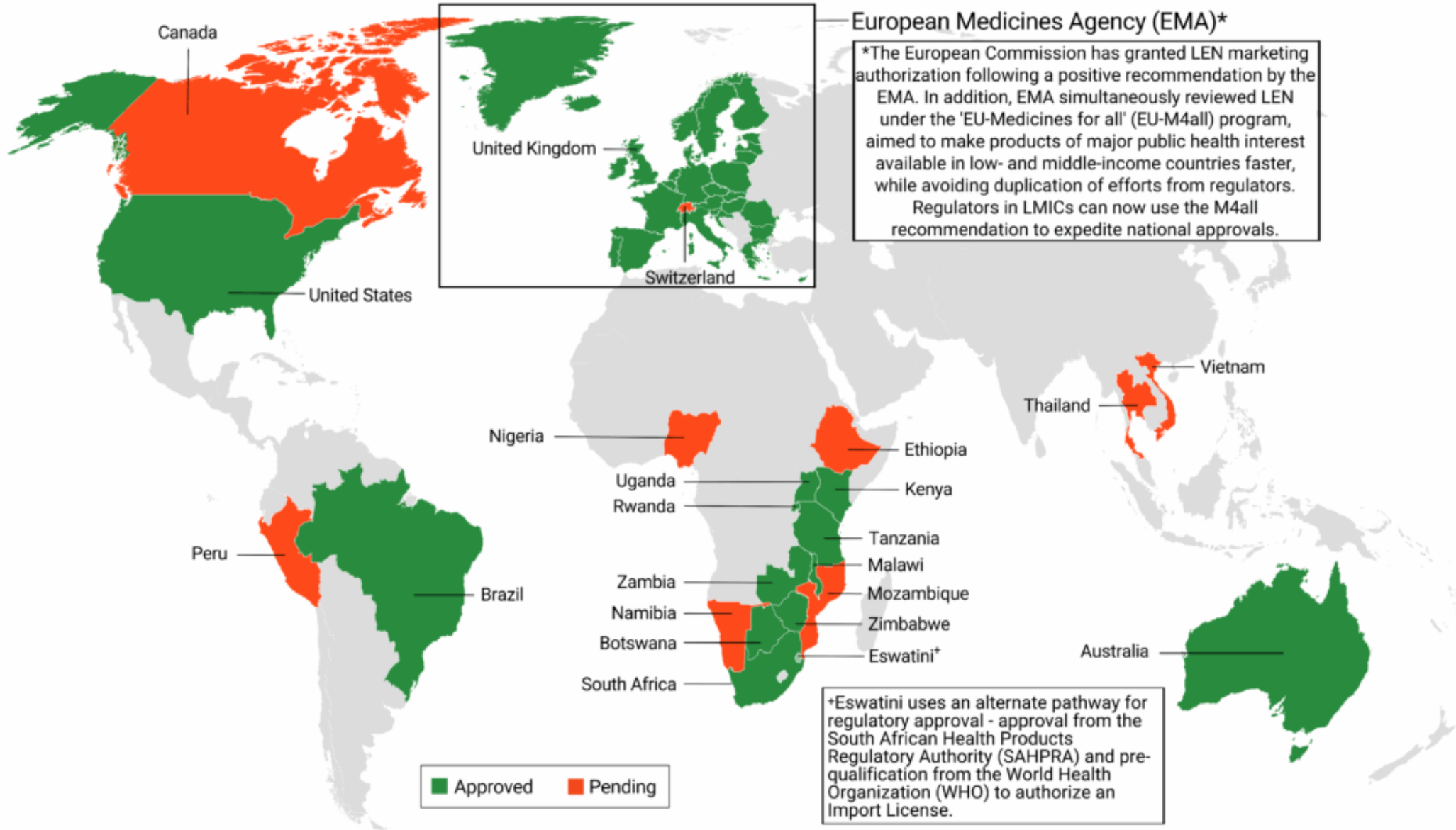


Updated Oct 2025

Trial	Population	Location	Size	2022	2023	2024	2025	2026	2027	2028	
 PURPOSE 1 Phase 3 Injectable lenacapavir & oral F/TAF	Cisgender adolescent girls and young women	South Africa and Uganda	5,345	Initial results released in June 2024 demonstrated no infections in the LEN arm							
 PURPOSE 2 Phase 3 Injectable lenacapavir	Cisgender men who have sex with men, Transgender women, Transgender men, Gender non- binary	US, South Africa, Peru, Brazil, Mexico, Argentina, and Thailand	3,271	Initial results released in September 2024 demonstrated LEN reduced HIV infections by 96% compared to background HIV incidence						 Update	
 PURPOSE 3 HPTN 102 Phase 2 Injectable lenacapavir	Cisgender women	US	253			Currently recruiting; estimated study completed date early 2028					
 PURPOSE 4 HPTN 103 Phase 2 Injectable lenacapavir	People who inject drugs	US	181			Currently recruiting; estimated study completed date mid-2027					
 PURPOSE 5 Phase 2 Injectable lenacapavir	Cisgender men who have sex with men, Transgender women, Transgender men, Gender non- binary	France, and UK	268			Enrollment expected to begin in the second half of 2024					
 PURPOSE 365 Phase 3 Injectable lenacapavir	Diverse population of people who would benefit from PrEP	US	300				Currently recruiting; estimated study completion date 2028				

Lenacapavir Regulatory Approval

14 regulatory approvals, **9** pending approvals as of January 2026



Efficacy trials of MK-8527

- MK-8527 is a novel, oral nucleoside reverse transcriptase translocation inhibitor (NRTTI)
- Potent; single dose of 0.5 mg reduced HIV-1 RNA by $\geq 1.0 \log_{10}$ copies/mL by Day 7
- Rapid onset of activity (30-60 min) to achieve levels associated with protection *in vitro*
- Monthly dosing feasible due to half-life of active MK-8527-TP of ~94-266 hrs
- Well-tolerated and no dose-related AEs in Phase 1 and 2 studies



EXPRESSIVE

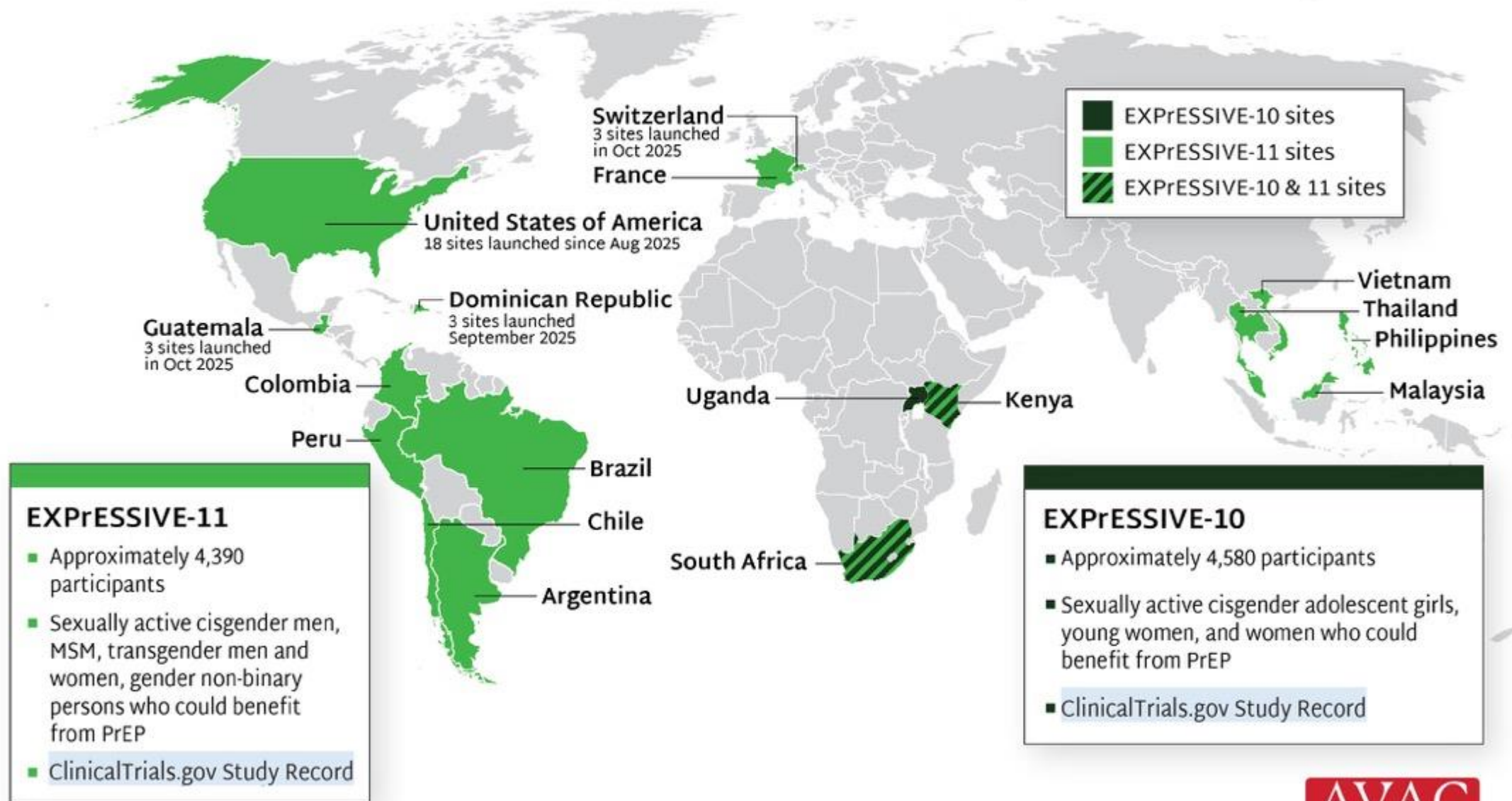
Efficacy

- MK-8590 transconcentrated
- Potent RNA binding
- Rapidly cleared from levels
- Monthly active
- Well-tolerated Phase

A potent, safe, immediate- & long-acting oral PrEP/PEP agent could be a game changer, facilitating community delivery & increase uptake, persistence & coverage

EXPrESSIVE Phase 3 Trial Countries of **MK-8527**

Seventeen countries in total are hosting sites for Merck's Phase 3 trials of the monthly PrEP pill, MK-8527. EXPrESSIVE-11 launched in August 2025; EXPrESSIVE 10 is expected to launch in Q4.





One last climb: WA hiker becomes oldest woman to summit Mount Rainier

July 29, 2023 at 6:00 am

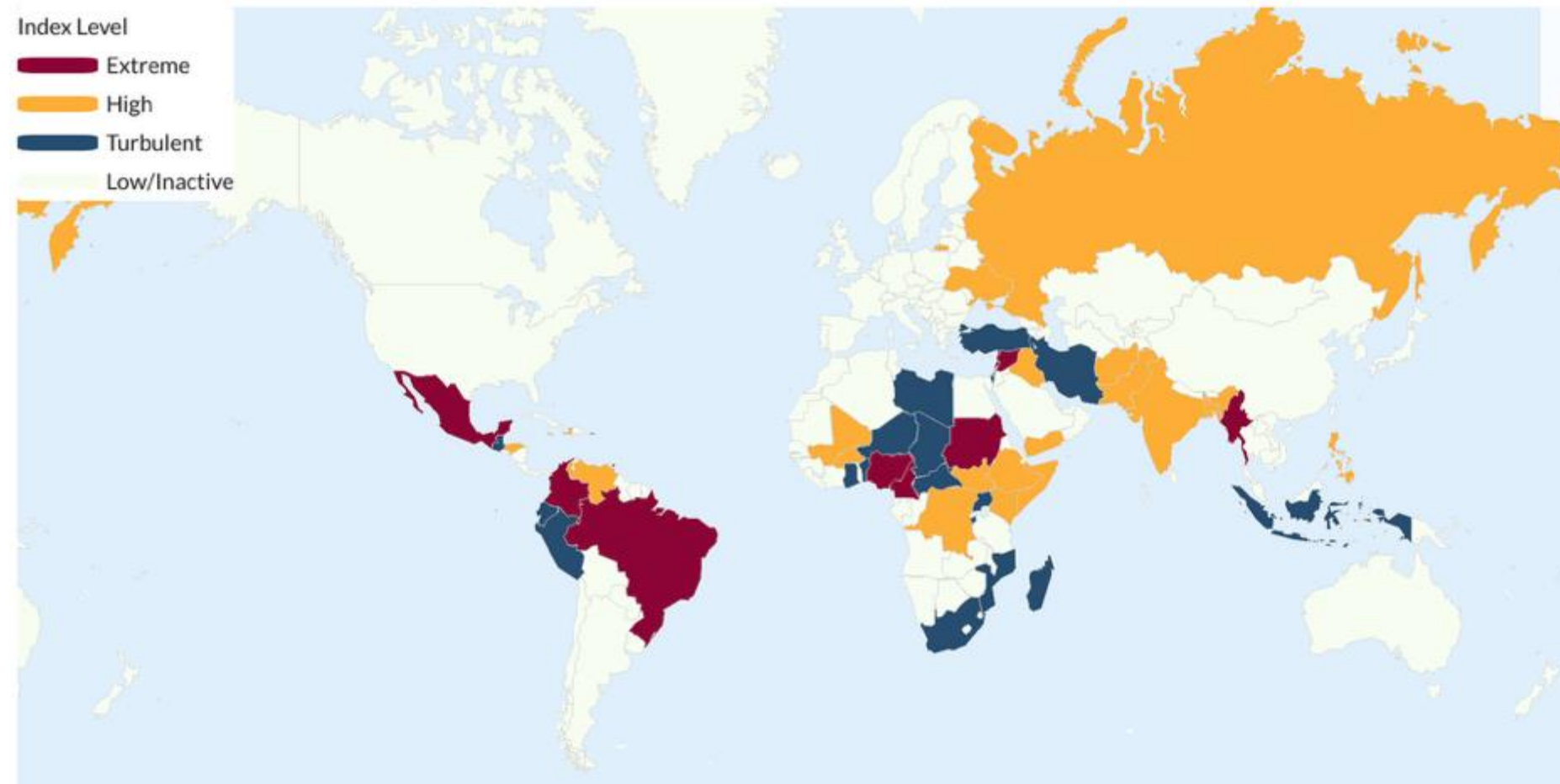


Is It Time to Declare Victory?

- Resistance?
- Distribution
 - Time to market
- Access
- Cost
- Demand
- Delivery infrastructure
- Assumptions on maintaining viral suppression in PLWH

- Delivery of any prevention product requires a stable, accessible infrastructure where the product can be stored safely and administered by trained workers

<https://acleddata.com/conflict-index/>



IN CONFLICT-AFFECTED COUNTRIES, ARE THE CONDITIONS FOR WOMEN WORSENING , STATIC , OR IMPROVING ?

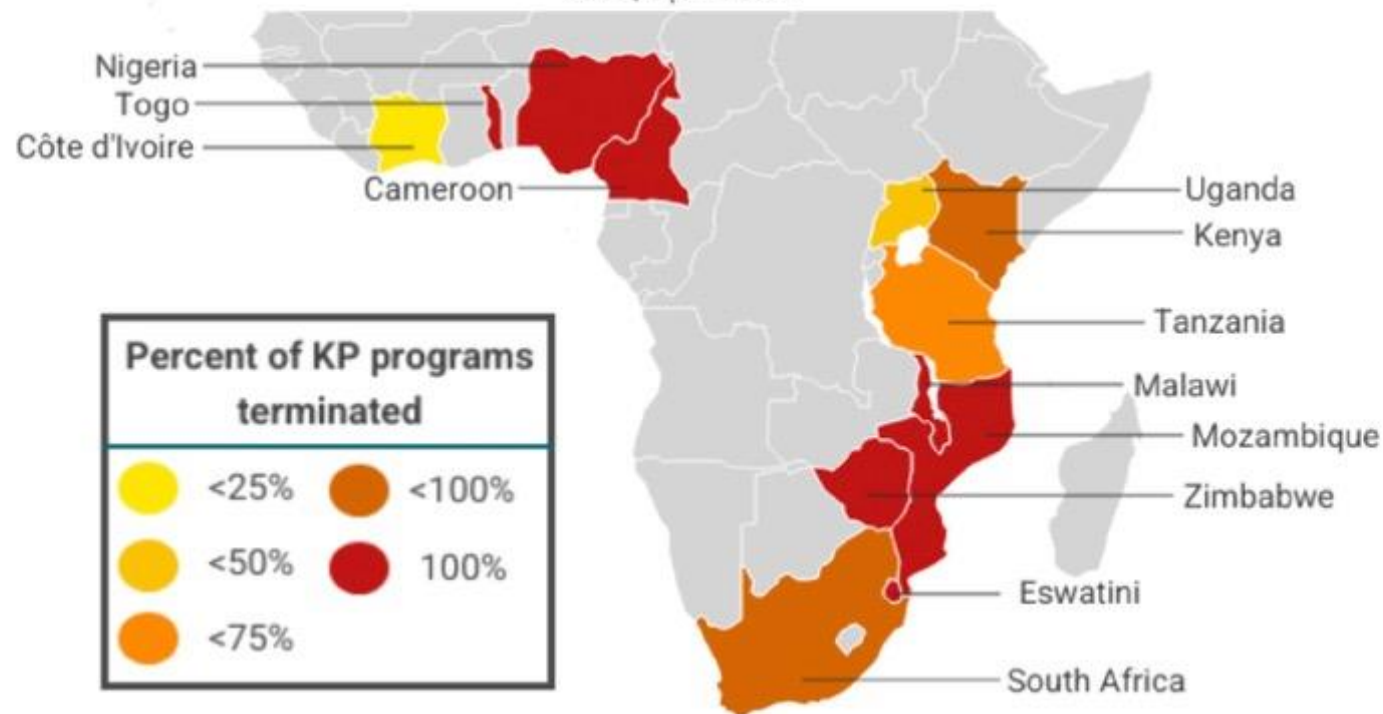
As of June 2024



... and people who are already more vulnerable suffer the most

Impact of US Funding Cuts on Services for Key Populations

Percentage of KP-serving implementing partners that have reported full or partial termination of the provision of KP services due to US funding cuts, April 2025



Global Black Gay Men Connect (GBGMC): Tracking the Freeze: Real-Time Impact on Key Populations,
<https://gbgmc.org/impact-us-funding-cuts/>.

Estimated deaths associated with the funding freeze and discontinuation
between January 24th, 2025 at 12:00 PM EST and present

Jan 19, 2026

Estimated adult deaths

157,120

Incrementing every 3.3 minutes

Estimated child deaths

16,725

Incrementing every 31 minutes

How many lives can be **saved** if all services are fully restored by the end of 2025?

Preventable adult deaths

0

Decrementing every 3.3 minutes

Preventable child deaths

0

Decrementing every 31 minutes

For all trackers above, we use average rates to estimate impact. In reality, these effects may vary over time, potentially starting smaller and accelerating as the situation progresses.

More CHOICES

Some sexual encounters may be infrequent, not planned, or not consensual

On-demand products can fill a gap; oral PrEP (2:1:2 F/TDF recommended for cisgender GBMSM)

Modeling suggests alternative F/TDF regimens might be appropriate in women, e.g. 2:1:1 on demand dosing

HPTN 106 will evaluate extended safety, acceptability, pharmacology of TFV rectal douche versus on- demand oral F/TDF in a randomized crossover study



DOI: 10.1093/infdi/jiae211

A Phase 1 Clinical Trial to Assess the Safety and Pharmacokinetics of a Tenofovir Alafenamide/Elvitegravir Insert Administered Rectally for HIV Prevention

Sharon A. Riddler,^{1,6} Clifton W. Kelly,² Craig J. Hoesley,^{3,4} Ken S. Ho,¹ Jeanna M. Piper,⁵ Stacey Edick,¹ Faye Heard,³ Gustavo F. Doncel,⁶ Sherri Johnson,⁷ Peter L. Anderson,^{4,6} Rhonda M. Brand,^{1,9} Ratiya Pamela Kunjara Na Ayudhya,⁹ José A. Bauermeister,¹⁰ Sharon L. Hillier,^{9,11} and Craig W. Hendrix¹², MTN-039 Protocol Team

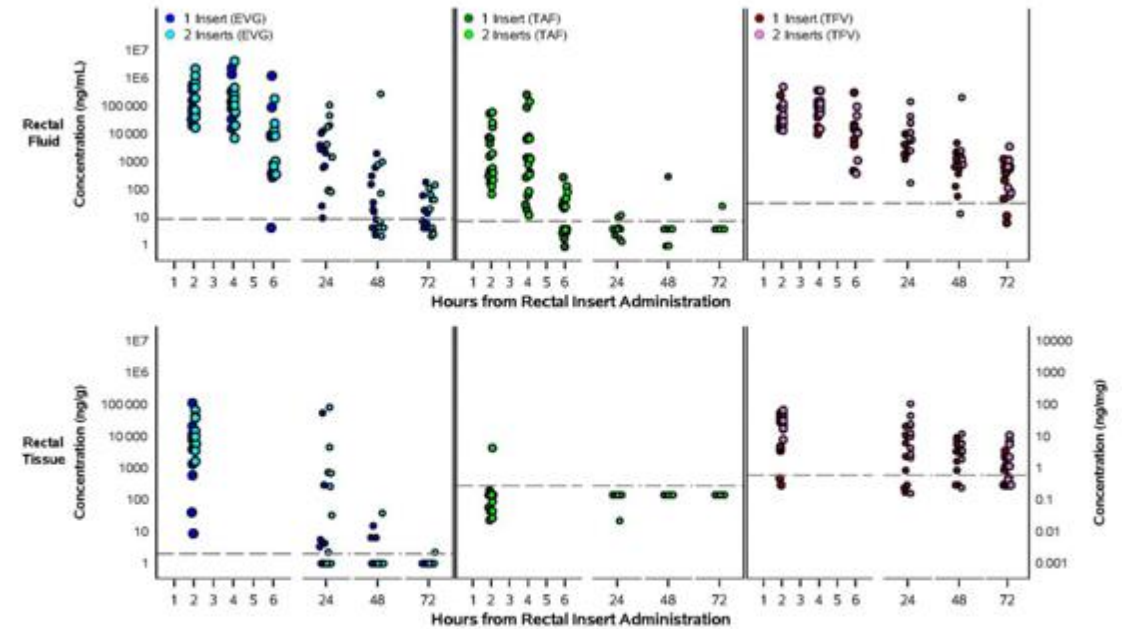


Figure 2. EVG, TAF, and TPV concentrations in rectal fluid and rectal tissue homogenates following rectal administration of 1 and 2 TAF/EVG (20 mg/16 mg) inserts. The median LLOQ for each analyte and sample type is indicated with a dashed line. The individual LLOQ varies with rectal swab fluid elution weight and rectal tissue biopsy weight, respectively. Concentrations below the LLOQ were set to one-half of the median LLOQ. Abbreviations: LLOQ, lower limit of quantification; EVG, elvitegravir; TAF, tenofovir alafenamide; TPV, tenofovir.

Rectal administration achieved high rectal tissue concentrations of EVG and TFV-DP with low systemic drug exposure & demonstrable ex vivo inhibition of HIV infection for 72 hours

Challenges, Old & New

Recognition of a complex landscape involving other infections & non-communicable diseases

Old

- Stigma
- Complacency
- Reliance on a homogenous portfolio (USG)
- “Slow” progress on HIV vaccine front
- Limited coverage w/ PEPFAR, with incomplete viral suppression & stubbornly high perinatal transmission in non-PEPFAR countries
- Threats to delivery infrastructure: politics, natural disasters, conflict

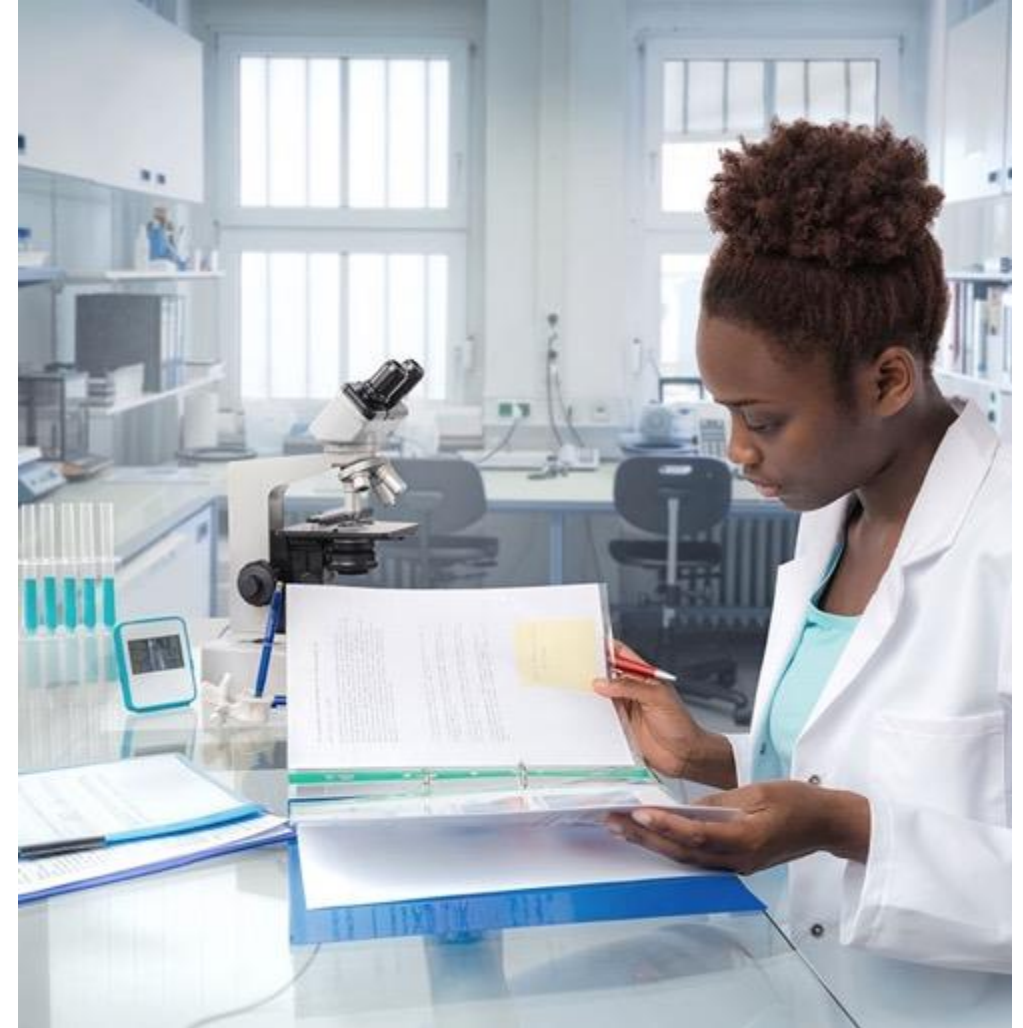
New



- Dramatic reduction in USG funding (NIH, USAID)
- Requirements for compliance with “new” priorities (language & populations)
- Interruptions in clinical trials & related research → erosion of community trust
- Complex administrative requirements to restore international funding from US
- Deprioritization of basic science research: implications for vaccine & cure

Equally Devastating

- Interruption of the pipeline of talent who will lead the next generation of STI/HIV prevention science, especially outside U.S.
- Isolationism leads to a loss of “global citizen” perspective
- Messages of compassion, hope, possibility





The Way Forward

- Communication
 - HIV still kills one person every minute on this planet
 - We are on the cusp of major breakthroughs—discovery & implementation—that we can't pull back from
- Diversification of funding sources
 - Reliable, longstanding sources no longer assured
 - Other governments, foundations, industry
- Maintain recognition of people more likely to acquire HIV, through multiple mechanisms; resist erasure!
- Respect individual choices

Honest Conversations



- Recognize that the HIV field has been uniquely (and understandably) favored with what seemed like unlimited funding for decades
- Confront the need to sustain investment, but be willing to prioritize & demonstrate efficiency
- Invoke community knowledge, strength & preferences to help advocate for & prioritize research

[illegible]